REMARKS

Claims 1-10, 121 and 123-130 are pending.

Claim Rejections -- 35 U.S.C. 112, First Paragraph

Applicants respectfully traverse the rejections of claims 1 and 3 as failing to comply with the written description requirement. The Office Action alleges that there "is no antecedent basis for the upper and lower layer yet one layer has a volume negligible compared to the volume of the other layer. The amendment in the two claims are self conflicting because if two layers are formed, they must have substantial volume of each layer. One can be less than the other but not "negligible" since such cannot be a two layer system." Applicants note that the recitation, "adding a C_5 to C_{12} saturated hydrocarbon to the remaining THF to form an upper layer and a lower layer", in step c) of claim 1, as well as, the recitation, "wherein the volume of THF after THF removal in step b) is negligible compared to the volume of the hydrocarbon added in step c)", in claim 3 have descriptive support at least in the specification at page 8, lines 11-13 and 20-23. Thus, claims 1 and 3 comply with the written description requirement.

According to the Miriam-Webster Online Dictionary, "negligible" is defined as "so small or unimportant or of so little consequence as to warrant little or no attention " (see http://www.m-w.com/dictionary/negligible). Claim 3 can be interpreted to mean that, after THF removal in step b), the volume of THF is very small compared to the volume of the hydrocarbon added in step c). However, even though the volume of THF is very small compared to the volume of the hydrocarbon added, there can still be two layers: a much larger layer of the hydrocarbon and a much smaller layer of THF. Withdrawal of the rejections is requested.

Rejections Under 35 U.S.C. §103

I. Applicants respectfully traverse the obviousness rejections of claims 6-9 over Kumar (WO 00/71124) in view of one of the following secondary references:

Hackh's Chemical Dictionary (pp. 693-694),

Lieberman (*Pharmaceutical Dosage Forms*, Volume 2, Second Edition, pp. 110-111, edited by Lieberman et al., 1990, Marcel Dekker Inc.),

Sekiguchi (CA 98:221701, abstract of Yakugaku Zasshi (1983) 103(2), 213-224), or

Leucuta (CA 98:113586, abstract of Clujul Medical (1982), 55(1), 60-66).

Kumar differs from claims 6-9 at least in not triturating a crude product in an ether or saturated hydrocarbon to obtain amorphous fexofenadine hydrochloride, wherein the crude

product is the product obtained after removing the organic solvent from a solution comprising fexonfenadine hydrochloride and an organic solvent.

Kumar discloses a process for preparing amorphous fexofenadine hydrochloride by dissolving fexofenadine hydrochloride in methanol, ethylacetate/methanol or acetone/methanol to obtain a clear solution; spray drying the solution with a spray dryer (Buchi Model 190) to isolate the amorphous fexofenadine hydrochloride (see Examples 1-3 of Kumar).

The Office Action relies on Hackh's definition of "triturate" as to grind particles for size reduction. The Office Action relies on Sekiguchi for disclosing the advantages of wet milling for size reduction of pharmaceutics. The Office Action relies on Lieberman for teaching "that size reduction in pharmaceutics is desirable since the smaller particle size will have formulation advantages" (pp. 110-111) and the Office Action relies on Leucuta for providing evidence of the effect in pharmaceutical products. Applicants note that Leucuta discloses that the in vitro dissolution rate of diazepam was increased when particles were highly dispersed or when the particle size was reduced by triturations in a mortar or ball mill. But Lieberman cautions in page 110 that: "It must be noted, however, that active ingredients reduced in particle size to gain the advantage of increased surface area, may not retain all of this advantage after being incorporated into a wet or dry granulation mix, and compressed into tablets." Lieberman also discloses that increasing the surface area may enhance an active ingredient's dissolution rate and hence, its bioavailability, which is particularly important with slightly soluble compounds, presumably in aqueous bodily media (p. 110). However, fexofenadine hydrochloride is not a slightly soluble compound in aqueous bodily media. So a person of ordinary skill in the art would not predict that size reduction for fexofenadine HCl powder would necessarily yield any formulation advantage.

Furthermore, applicants contend that, based on the disclosures of Hackh's, Lieberman, Sekiguich or Leucuta, the person of ordinary skill in the art would not have any reason to modify the process of Kumar by triturating, in an ether or saturated hydrocarbon, the product of the spray drying step of Kumar to obtain amorphous fexofenadine hydrochloride. This is because the person of ordinary skill would have understood that the spray drying process of Kumar already produces very fine powder of amorphous fexofenadine hydrochloride in very small size. Kumar used Buchi Model 190 as the spray drier. Eljamal (US 6,136,346 B1, issued on October 24, 2000) discloses that using Buchi Model 190 as the spray drier to spray dry pharmaceuticals produced pharmaceutical powder having a mass median diameter of 2.0 to 2.6 μm, wherein at least 60% of the particles in the powder had a diameter of 5 μm or less (see Tables 2 and 3 in columns 21 and 22). Lieberman discloses that a fine powder of phenacetin had better bioavailability than medium or coarse powder of phenacetin, wherein the fine powder was a powder having a particle size less than 75 μm, the medium powder had a particle size ranging from 150 to 180 μm, and the coarse

powder had a particle size greater than 250 μm (see Figure 2, page 111, Lieberman). Thus, the amorphous fexofenadine hydrochloride produced by Kumar's spray drying process would be expected to have a size much smaller than the 75 μm size that Lieberman found to lead to better bioavailability. Because the powder of amorphous fexofenadine hydrochloride produced by Kumar's process is already a very fine powder (being an order of magnitude smaller than 75 μm) based on the experience of Eljamal with Buchi Model 190 dry sprayer, the person of ordinary skill in the art would have no motivation or desirable reason for modifying the process of Kumar by triturating the very fine powder of amorphous fexonfenadine hydrochloride produced by the spray drying process of Kumar. The trituration step would be viewed as a labor intensive add-on which would not be expected to yield any benefit. Therefore, applicants contend that Hackh's, Lieberman et al., Sekiguchi et al. or Leucuta et al. does not cure the deficiencies of Kumar. Thus, despite the disclosures of Hackh's, Lieberman, Sekiguich or Leucuta, it would not have been obvious to modify the spray drying process of Kumar to arrive at the processes of claims 6-9.

II. Applicants respectfully traverse the rejections of claims 1-10, 121 and 123-130 as obvious over Kumar in view of Hackh's, Lieberman, Sekiguich or Leucuta, further in view of Okabe (Chemical Abstract, CA 114:54120, 1991) or Williams (US 6,862,890).

(A) Concerning claims 1-5:

Kumar differs from claims 1-5 at least in not performing the following steps:

a) preparing a solution of fexofenadine hydrochloride in THF;
b) removing a portion of THF from the solution;
c) adding a C_5 to C_{12} saturated hydrocarbon to the remaining THF to form an upper layer and a lower layer;
d) separating the upper layer from the lower layer; and
e) drying the lower layer to obtain the amorphous fexofenadine hydrochloride.

In the spray drying process of Kumar, fexofenadine hydrochloride is dissolved in a suitable solvent, wherein the term "suitable solvent" is rather broad meaning lower alkanol or combination of lower alkanol, ester, ketone, chlorinated solvent and mixtures thereof (page 4, lines 15-16). All the working examples of Kumar used methanol or methanol in combination with another polar organic solvent. Kumar does not disclose using any ether, let alone THF, as the suitable solvent. None of the secondary references, i.e., Hackh's, Lieberman, Sekiguich and Leucuta, cures the deficiencies of Kumar. The Office Action relies on Okabe for the disclosure that both spray dryer and evaporator are alternative apparatuses for solvent removal. The Office Action also relies on Williams for the disclosures that spray drying is a solvent removal procedure analogous to other conventional solvent removing procedures

(column 1, lines 26, 27 and 39; column 2, lines 59-60), and optionally ethanol, methanol or THF are choices of solvents (column 4, lines 51-56). However, as explained below, applicants contend that Williams does not provide sufficient guidance to replace methanol with THF as the solvent for dissolving fexofenadine hydrochloride.

Williams discloses a spray freezing process for preparing microparticles or nanoparticles of an effective ingredient, comprising dissolving the effective ingredient in a suitable solvent, spraying the solution under a cryogenic liquid to generate frozen particles containing the solvent and the effective ingredient, and drying the frozen particles to remove the solvent to obtain microparticles or nanoparticles of the effective ingredient. Williams' list of "effective ingredient" includes a huge number of substances:

> "Non-limiting examples of effective ingredients are pharmaceuticals, peptides, nucleic acids, proteins, antibiotics, gene therapy agents, catalysts, adsorbents, pigments, coatings, personal care products, abrasives, particles for sensors, metals, alloys, ceramics, membrane materials, nutritional substances, anti-cancer agents, as well as, chemicals used in the agriculture industries such as fertilizers, pesticides and herbicides. It will be appreciated that this list is not exhaustive and is for demonstrative purposes only. It will be further appreciated that it is possible for one compound to be included in more than one class of effective ingredients, for example, peptides and pharmaceuticals.
>
> Examples of pharmaceuticals include, but are not limited to, antibiotics, analgesics, anticonvulsants; antidiabetic agents, antifungal agents, antineoplastic agents, antiparkinsonian agents, antirheumatic agents, appetite suppressants, biological response modifiers, cardiovascular agents, central nervous system stimulants, contraceptive agents, diagnostic agents, dopamine receptor agonists, erectile dysfunction agents, fertility agents, gastrointestinal agents, hormones, immunomodulators, antihypercalcemia agents, mast cell stabilizers, muscle relaxants, nutritional agents, ophthalmic agents, osteoporosis agents, psychotherapeutic agents, parasympathomimetic agents, parasympatholytic agents, respiratory agents, sedative hypnotic agents, skin and mucous membrane agents, smoking cessation agents, steroids, sympatholytic agents, urinary tract agents, uterine relaxants, vaginal agents, vasodilator, anti-hypertensive, hyperthyroids, anti-hyperthyroids, anti-asthmatics and vertigo agents."

In claim 3, Williams discloses that the pharmaceutical can be "proteins, peptides, albuterol sulfate, terbutaline sulfate, diphenhydramine hydrochloride, chlorpheniramine maleate, loratidine hydrochloride, fexofenadine hydrochloride, phenylbutazone, nifedipine, carbamazepine, naproxen, cyclosporin, betamethosone, danazol, dexamethasone, prednisone, hydrocortisone, 17 beta-estradiol, ketoconazole, mefenamic acid, beclomethasone, alprazolam, midazolam, miconazole, ibuprofen, ketoprofen, prednisolone, methylprednisone, phenytoin, testosterone, flunisolide, diflunisal, budesonide, fluticasone; insulin, glucagon-like peptide, C-Peptide, erythropoietin, calcitonin, human growth hormone, luteinizing hormone, prolactin, adrenocorticotropic hormone, leuprolide, interferon alpha-2b, interferon beta-1a, sargramostim, aldesleukin, interferon alpha-2a, interferon alpha-n3alpha, proteinase inhibitor; etidronate, nafarelin, chorionic gonadotropin, prostaglandin E2, epoprostenol, acarbose, metformin, or desmopressin, cyclodextrin, antibiotics; and the pharmacologically acceptable organic and inorganic salts or metal complex thereof." As seen above, the list of pharmaceuticals in claim 3 of Williams is very broad because "proteins", "peptides", "proteinase inhibitor" and "antibiotics" can be a large number of pharmaceutical entities.

The list of solvents that can be used in the process of Williams is extremely broad: "an aqueous such as water, one or more organic solvents, or a combination thereof. When used, the organic solvents can be water soluble or non-water soluble. Suitable organic solvents include but are not limited to ethanol., methanol, tetrahydrofuran, acetonitrile, acetone, tert-butyl alcohol, dimethyl sulfoxide, N,N-dimethyl formamide, diethyl ether, methylene chloride, ethyl acetate, isopropyl acetate, butyl acetate, propyl acetate, toluene, hexanes, heptane, pentane, and combinations thereof." The examples of suitable organic solvents include polar and non-polar organic solvents. The solvent list includes just about any solvents with divergent or, in some case, opposite properties (aqueous solvents and organic solvents can be the solvents; water soluble organic solvents, non-water soluble organic solvents, polar organic solvents and non-polar organic solvents can also be the solvents). Thus, based on the very broad disclosure of Williams, the person of ordinary skill in the art would not have been guided to use THF to dissolve the effective ingredient in the spraying method to obtain nanoparticles or microparticles of the effective ingredient. With this universal list of solvents, coupled with the large number of effective ingredients disclosed by Williams, applicants submit that a person of ordinary skill in the art would not have selected THF to replace methanol as the solvent for fexofenadine hydrochloride based on the disclosures of Williams because Williams does not provide any guidance toward selecting THF or methanol from the universal list of solvents and selecting fexofenadine hydrochloride from the extremely long list of effective ingredients. The person of ordinary skill in the art would not have predicted that using THF to dissolve fexofenadine hydrochloride in the spray drying method would have a reasonable expectation of success.

The other secondary reference, i.e., Okabe (CA 114:54120) relied upon by the Office Actions also does not provide any guidance of replacing methanol in the spray drying process of Kumar with THF. This is because Okabe merely discloses a process for manufacturing oxide ceramics comprising (1) adding aqueous ammonia to a solution containing at least nitrates and/or hydrides of mono- or divalent metals and divalent to hexavalent metals; (2) removing the solvent by using a spray dryer; (3) drying, pre-sintering, and mixing with an oxide; and (4) sintering to form the oxide ceramic. Okabe is silent on fexofenadine hydrochloride and THF. Thus, in view of Hackh's, Lieberman, Sekiguich or Leucuta, further in view of Okabe or Williams, applicants contend that it would not have been obvious to modify the spray drying process of Kumar by dissolving fexofenadine hydrochloride in THF instead of "lower alkanol or combination of lower alkanol, ester, ketone, chlorinated solvent and mixtures thereof."

Even if, for argument purposes, it is assumed that the person of ordinary skill in the art were to use THF as the solvent to dissolve fexofenadine hydrochloride in the spray drying process of Kumar, none of the secondary reference, Hackh's, Lieberman, Sekiguich or Leucuta, in view of Okabe or Williams would have led the person of ordinary skill in the art to predict that modifying the spray drying process of Kumar by adding the following steps would have a reasonable expectation of success:

b) removing a portion of THF from the solution;

c) adding a C_5 to C_{12} saturated hydrocarbon to the remaining THF to form an upper layer and a lower layer; and

d) separating the upper layer from the lower layer.

Especially, because Hackh's, Lieberman, Sekiguich or Leucuta, further in view of Okabe or Williams, are silent on performing steps b), c) and/or d).

Even if, for argument purposes, it is assumed that the person of ordinary skill in the art were to use THF as the solvent to dissolve fexofenadine hydrochloride in the spray drying process of Kumar, after dissolving the fexofenadine hydrochloride in THF, the person of ordinary skill would directly put the fexofenadine hydrochloride THF solution in the Buchi Model 190 spray drier to generate the amorphous fexofenadine hydrochloride ultrafine powder. There would have been no valid reason to incur extra time, labor and cost by removing a portion of THF from the solution; adding a saturated hydrocarbon to the remaining solution to form an upper layer and a lower layer; and separating the upper layer from the lower layer.

Withdrawal of the obviousness rejections of claims 1-5 is requested.

(B) Concerning claims 6-10, 121 and 123-130:

Claims 6-10, 121 and 123-130 differ from Kumar at least in that Kumar does not triturate the product of the spray drying in ether or saturated hydrocarbon to form the amorphous fexofenadine hydrochloride. Hackh's, Lieberman, Sekiguich or Leucuta does not cure the deficiencies of Kumar. Okabe or Williams does not provide any motivation to modify the spray drying process of Kumar by adding the triturating step. As explained above, the powder of amorphous fexofenadine hydrochloride prepared by the spray drying process of Kumar is already very fine and need no further particle size reduction by trituration. In addition, Hackh's, Lieberman, Sekiguich or Leucuta, further in view of Okabe or Williams, is silent on trituration.

Withdrawal of the obviousness rejections of claims 6-10, 121 and 123-130 over Kumar in view of Hackh's, Lieberman, Sekiguich or Leucuta, further in view of Okabe or Williams is requested.

III. Applicants respectfully traverse the obviousness rejections of claims 1-10 and 121-131 over one of these primary references:

Carr '129 (US 4,254,129),
Carr '957 (US 4,285,957),
WO 95/31437 (hereinafter "Henton") or
Woosley (US 5,375,693),

in view of the following secondary references:

Lieberman (*Pharmaceutical Dosage Forms*, Volume 2, Second Edition, pp. 110-111, edited by Lieberman et al., 1990, Marcel Dekker Inc.),

Suzuki (Chemical Abstract, CA 91:44479, abstract of Chemical & Pharmaceutical Bulletin (1979), 27(5), 1214-1222),

Corrigan (Chemical Abstract, CA 98:166814, abstract of Drug Development and Industrial Pharmacy (1983), 9 (1-2), 1-20),

Nuernberg (Chemical Abstract, CA 86:8603, abstract of Progress in Colloid & Polymer Science (1976), 59, 55-69), and

Sato (Chemical Abstract, CA 110:179429, abstract of Yakuzaigaku (1988), 48(4), 296-304), supplemented with

US '127 (US 5,990,127)

for the reasons of record.

(A) Rejections Based on Carr '129 or Carr '957 as Primary Reference:

Because Carr '957 is a division of Carr '129, the following discussion will use Carr '129 as the representative. The previous Office Action dated December 16, 2005 alleges that Carr '129 discloses fexofenadine hydrochloride in column 13, Example 3. However, applicants note that Example 3 of Carr '129 prepared fexofenadine free base, not

fexofenadine hydrochloride (see column 13, lines 36-37). In addition, Example 3 of Carr '129 prepared the crystals of fexofenadine free base by recrystallization of the free base from methanol-butanone (column 13, lines 34-35).

Carr '129 differs from claims 1-5 at least in not disclosing a process for preparing amorphous fexofenadine hydrochloride comprising the following steps:

a) preparing a solution of fexofenadine hydrochloride in THF;
b) removing a portion of THF from the solution;
c) adding a C_5 to C_{12} saturated hydrocarbon to the remaining THF to form an upper layer and a lower layer;
d) separating the upper layer from the lower layer; and
e) drying the lower layer to obtain the amorphous fexofenadine hydrochloride.

Lieberman discloses that size reduction of solid pharmaceuticals may offer certain advantages in tablet formula development such as (1) an increase in surface area may enhance an active ingredient's dissolution rate, but this advantage may not be retained after being incorporated into a granulation mix and compressed into tablets, and (2) improved tablet content uniformity due to more particles of the active ingredient available (see page 110). Suzuki discloses that the freeze drying of griseofulvin in a benzene system resulted in a solvate powder having an average size in the submicron level, and upon the addition of surfactants to the freeze drying process, micronized particles were obtained with improved dissolution rate of griseofulvin. Corrigan discloses that spray drying phenobarbital or hydroflumethiazide with 10% Plasdone C-15 (PVP) resulted in amorphous phenobarbital or hydroflumethiazide, respectively, having increased solubility than crystalline phenobarbital or hydroflumethiazide. Nuernberg discloses that spray dried drugs were more soluble than the crystalline forms of the drugs due to production of amorphous forms. Sato discloses that freeze drying a solution of 9,3"-diacetylmidecamycin in dioxane produced a pure amorphous solid of 9,3"-diacetylmidecamycin, while grinding in a vibration mill up to 20 hours failed to produce a pure amorphous solid, and the solubility of the freeze dried amorphous 9,3"-diacetylmidecamycin was almost the same as the spray dried amorphous 9,3"-diacetylmidecamycin reported before. US '127 discloses a process of preparing fexofenadine free base by incubating a phosphorylated derivative of the fexofenadine free base dissolved in DMF or ethanol with certain strains of *Cunninghamella* fungus; treating an aliqout of the culture with 50% methanol to obtain a suspension; centrifugating the suspension at 10,000 g to obtain a clear supernatant; and analyzing the clear supernatant with HPLC to obtain the fexofenadine free base (see Examples 4 and 5 in columns 5-6). Thus, Lieberman, Suzuki, Corrigan, Nuernberg, Sato and US '127 do not disclose steps a) to e) of claim 1. In fact, Lieberman, Suzuki, Corrigan, Nuernberg, Sato and US '127 do not even disclose the preparation of amorphous fexofenadine hydrochloride. As a result, Lieberman, Suzuki,

Corrigan, Nuernberg, Sato and US '127 fail to cure the deficiencies of Carr '129 concerning claims 1-5. Claims 1-5 would not have been obvious over Carr '129 or Carr '957 in view of Lieberman, Suzuki, Corrigan, Nuernberg, and Sato supplemented with US '127.

Carr '129 discloses the preparation of crystalline fexofenadine free base, not amorphous fexofenadine hydrochloride (Example 3 in column 13). Carr '129 differs from claims 6-10, 121 and 123-130 at least in not teaching

a) preparing a solution of fexofenadine hydrochloride in an organic solvent, such as methanol, ethanol, isopropanol and/or acetone; and
b) removing the solvent from the solution to obtain a crude product; and
c) triturating the crude product in an ether or saturated hydrocarbon to obtain the amorphous fexofenadine hydrochloride.

Lieberman, Suzuki, Corrigan, Nuernberg, and Sato supplemented with US '127 do not disclose any process to prepare amorphous fexofenadine hydrochloride. Thus, Lieberman, Suzuki, Corrigan, Nuernberg, and Sato supplemented with US '127 fail to remedy the deficencies of Car '129. Claims 6-10, 121 and 123-120 would not have been obvious over Carr '129 or Carr '957 in view of Lieberman, Suzuki, Corrigan, Nuernberg, and Sato supplemented with US '127.

(B) Rejections Based on WO 95/31437 (Henton) as Primary Reference

Henton discloses 4 crystalline forms of fexofenadine hydrochloride (anhydrous Forms I and III; hydrated Forms II and IV; see page 5 line 1 to page 8, line 15) prepared by recrystallization from suitable solvents. Henton is silent on amorphous fexofenadine hydrochloride. Henton differs from claims 1-5 at least in not disclosing:

a) preparing a solution of fexofenadine hydrochloride in THF;
b) removing a portion of THF from the solution;
c) adding a C_5 to C_{12} saturated hydrocarbon to the remaining THF to form an upper layer and a lower layer;
d) separating the upper layer from the lower layer; and
e) drying the lower layer to obtain the amorphous fexofenadine hydrochloride.

Lieberman, Suzuki, Corrigan, Nuernberg, and Sato supplemented with US '127 do not disclose any process to prepare amorphous fexofenadine hydrochloride. Lieberman, Suzuki, Corrigan, Nuernberg, and Sato supplemented with US '127 are silent as to steps a)-e) of claim 1. Thus, Lieberman, Suzuki, Corrigan, Nuernberg, and Sato supplemented with US '127 fail to remedy the deficencies of Henton. Claims 1-5 would not have been obvious over Henton in view of Lieberman, Suzuki, Corrigan, Nuernberg, and Sato supplemented with US '127.

Henton differs from claims 6-10, 121 and 123-130 at least in not disclosing triturating a crude produce comprising fexofenadine hydrochloride in an ether or saturated hydrocarbon to obtain amorphous fexofenadine hydrochloride. Lieberman, Suzuki, Corrigan, Nuernberg, and Sato supplemented with US '127 do not disclose any process to prepare amorphous fexofenadine hydrochloride. Lieberman, Suzuki, Corrigan, Nuernberg, and Sato supplemented with US '127 are silent as to step c) of claim 6 or 125. Thus, Lieberman, Suzuki, Corrigan, Nuernberg, and Sato supplemented with US '127 fail to remedy the deficencies of Henton. Claims 6-10, 121 and 123-130 would not have been obvious over Henton in view of Lieberman, Suzuki, Corrigan, Nuernberg, and Sato supplemented with US '127.

(C) Rejections Based on Woosley (US 5,375,693) as Primary Reference

Woosley discloses terfenadine, i.e., methyl 4-[1-hydroxy-4-(4-hydroxydiphenylmethyl-1-piperidinyl)-butyl]-α,α-dimethylbenzeneacetate, useful as an antihistamine (column 3, lines 25-34). Woosley is totally silent on fexofenadine, let alone amorphous fexonfenadine hydrochloride. Woosley differs from claims 1-5 at least in not disclosing

a) preparing a solution of fexofenadine hydrochloride in THF;
b) removing a portion of THF from the solution;
c) adding a C_5 to C_{12} saturated hydrocarbon to the remaining THF to form an upper layer and a lower layer;
d) separating the upper layer from the lower layer; and
e) drying the lower layer to obtain the amorphous fexofenadine hydrochloride.

Lieberman, Suzuki, Corrigan, Nuernberg, and Sato supplemented with US '127 do not disclose any process to prepare amorphous fexofenadine hydrochloride. Lieberman, Suzuki, Corrigan, Nuernberg, and Sato supplemented with US '127 are silent as to steps a)-e) of claim 1. Thus, Lieberman, Suzuki, Corrigan, Nuernberg, and Sato supplemented with US '127 fail to remedy the deficencies of Woosley. Claims 1-5 would not have been obvious over Woosley in view of Lieberman, Suzuki, Corrigan, Nuernberg, and Sato supplemented with US '127.

Woosley differs from claims 6-10, 121 and 123-130 at least in not disclosing:

a) preparing a solution of fexofenadine hydrochloride in an organic solvent, such as methanol, ethanol, isopropanol and/or acetone; and
b) removing the solvent from the solution to obtain a crude product; and
c) triturating the crude product in an ether or saturated hydrocarbon to obtain the amorphous fexofenadine hydrochloride.

Lieberman, Suzuki, Corrigan, Nuernberg, and Sato supplemented with US '127 do not disclose any process to prepare amorphous fexofenadine hydrochloride. Thus, Lieberman, Suzuki, Corrigan, Nuernberg, and Sato supplemented with US '127 fail to remedy the deficencies of Woosley. Claims 6-10, 121 and 123-120 would not have been obvious over Woosley in view of Lieberman, Suzuki, Corrigan, Nuernberg, and Sato supplemented with US '127.

In view of the reasons above, withdrawal of all the obviousness rejections is requested.

Rejections under 35 U.S.C. §102(e) or (g)

Applicants respectfully traverse the provisional anticipatory rejections of claims 1-10, 121 and 123-130 under 35 U.S.C. 102(e) or (g) over US 2005/0165056 (hereinafter referred to as "Kirsch").

The Office Action relies on page 2, examples 5 and 6, and page 3, claims 15-19, of Kirsch. Applicants contend that claims 1-10, 121 and 123-130 are not anticipated by Kirsch under 35 U.S.C. 102(e) because Kirsch is not prior art under 35 U.S.C. 102(e). Since Kirsch is a U.S. national phase application of a PCT application filed after November 29, 2000, but not published in English, Kirsch is NOT prior art under 35 U.S.C. 102(e) (please see MPEP 706.02(f)(1), Example 5). The effective prior art date of Kirsch is its publication data, July 28, 2005. But the present application, Serial No. 10/661,259 is a division of U.S. Application Serial No. 10/118,807 filed on April 8, 2002. Thus, the effective filing date of the present application predates the effective prior art date of Kirsch. The Office Action asserts that Kirsch is entitled to priority benefit of a NAFTA country. However, applicants note that Kirsch claims priority to a Switzerland patent application, and that Switzerland is not a NAFTA country. As a result, the provisional anticipatory rejection of claims 1-10, 121 and 123-130 under 35 U.S.C. 102(e) over Kirsch should be withdrawn.

With regard to the provisional anticipation rejection under 35 U.S.C. 102(g), applicants do not acquiescence to whether an interference would establish that Kirsch invented the claimed processes before applicants without abandonment, suppression or concealment. However, the provisional anticipatory rejection of claims 1-10, 121 and 123-130 under 35 U.S.C. 102(g) over Kirsch should be withdrawn because Kirsch fails to claim every limitations of claims 1-10, 121 and 123-130. Kirsch discloses a process for preparing amorphous, non-hydrated fexofenadine hydrochloride by:

suspending fexofenadine free base in a lower alkane, di(lower alkyl) ether or a lower alkyl ester of a lower alkanecarboxylic acid;

adding a solution of hydrogen chloride in a lower alkanol, di(lower alkyl) ether or a lower alkyl ester of a lower alkanecarboxylic acid to form a mixture;

heating the mixture;

cooling the heated mixture; and

isolating the amorphous, non-hydrated fexofenadine hydrochloride from the cooled mixture (see claims 15-19).

Kirsch differs from claims 1-5 at least in not claiming a process with the following steps:

a) preparing a solution of fexofenadine hydrochloride in THF;

b) removing a portion of THF from the solution;

c) adding a C_5 to C_{12} saturated hydrocarbon to the remaining THF to form an upper layer and a lower layer;

d) separating the upper layer from the lower layer; and

e) drying the lower layer to obtain the amorphous fexofenadine hydrochloride.

Thus, Kirsch fails to provisionally anticipate claims 1-5.

Kirsch also differs from claims 6-10, 121 and 123-130 at lest in not claiming process with the following steps:

b) removing the solvent such as methanol, ethanol, isopropanol and/or acetone from the solution of fexofenadine hydrochloride in the solvent to obtain a crude product; and

c) triturating the crude product in an ether or saturated hydrocarbon to obtain the amorphous fexofenadine hydrochloride.

Thus, Kirsch also fails to provisionally anticipate claims 6-10, 121 and 123-130.

Due to at least the above reasons, withdrawal of the provisional anticipatory rejections of claims 1-10, 121 and 123-130 over Kirsch is requested.

Conclusion

Applicants submit that the application is in condition for allowance. If there remains any minor issues that can be resolved via a telephone interview, the Examiner is urged to call the undersigned to expedite the allowance of the application.

Respectfully submitted,

KENYON & KENYON LLP

Dated: November 21, 2007

By: King L. Wong
King L. Wong
Reg. No. 37,500

One Broadway
New York, New York 10004
(212) 425-7200 (telephone)
(212) 425-5288 (facsimile)

CUSTOMER NUMBER 26646